Remarks

I. Objection to the Specification

The Examiner suggests a new title on the grounds that the title as originally filed is not descriptive.

The Examiner made the same objection in the Office Action dated July 23, 2002. In response, Applicants amended the title to "Antiviral Therapy Using Ovine Interferon Tau" in the response mailed November 25, 2002. Should the Examiner find the title as previously amended not descriptive of the invention, Applicants will again amend the title.

II. Rejections Under 35 U.S.C. § 112, first paragraph

Claims 66-71 and 97 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention.

Claim 67 was rejected under 35 U.S.C. § 112, first paragraph, as allegedly non-enabling for inhibiting Hepatitis C viral replication.

Applicants respectfully traverse these rejections.

A. Rejection of Claims 66-71 and 97 as Non-Enabled

In establishing the rejection of claims 66-71 and 97 as non-enabling, the Examiner makes several assertions that are addressed individually.

1. The Examiner's First Assertion

It is the Examiner's position that the claims are not enabled because, while Applicant has shown *in vitro* data for the activity of interferon-τ, the prior art does not disclose that the models on which the data was obtained are acceptable models for *in vivo* treatment (Office Action, page 3, first full paragraph). In short, the Examiner asserts there is no evidence indicating that the cellular assays used are recognized models to study anti-viral effects of ovine interferon-τ (Office Action, page 3, first full paragraph).

In response, Applicants note that:

1. the anti-viral activity of interferon-τ was established and recognized by those of skill in the art as early as 1988;
2. the cellular assays used in Example 18 of the application to support the present claims are the same assays used by those of skill in the art;
3. the anti-viral activity of interferon-τ was evaluated *in vivo* by inoculating 24 newborn lambs with ovine lentivirus and treating a group of the lambs with intererfon-τ, as reported in Applicants' specification on page 35, lines 11-30; and
4. the M.P.E.P is quite clear in stating that "a rigorous or an invariable exact *in vitrolin vivo* correlation" is not the standard for compliance with enablement.

Each of these points is addressed in the following paragraphs.

With respect to the first and second points, the anti-viral activity of interferon-τ was reported by Pontzer *et al.* in 1988 in *Biochem. Biophys. Res. Comm.*, 152(2):801 (copy enclosed). A second paper by Pontzer appeared in 1990 in *Proc. Natl. Acad. Sci. USA* (87:5945 (1990)), also reporting on the anti-viral properties of interferon-τ (copy enclosed)[1]. In both papers, Pontzer *et al.* use the same antiviral assay utilized by the present applicants – inhibition of viral replication in Madin-Darby bovine kidney (MDBK) cells using vesicular stomatitis virus as the challenge virus (see Example 2 on page 63 and Example 10 on page 79 of the specification; see page 802 of Pontzer *et al.*-1988; see page 5946, Col. 1 of Pontzer *et al.*-1990).

Applicants specification additionally provides analysis of antiviral activity of interferon-τ in other cells lines, sheep normal fibroblasts (see Example 10 on page 79), peripheral blood mononuclear cells (Examples 11 and 12, pages 80, 82), and HepG2-T14 cells (a human hepatocyte cell line; Example 18, pages 98-101).

[1]The present application has a priority date of March 2, 1989. Thus, the 1990 paper by Pontzer *et al.* is not effective prior art. The 1988 paper by Pontzer *et al.* was published in April 1988. Thus, the document is not a §102(b) reference. Nor does the document qualify as prior art under §102(a), since Pontzer is an named inventor and an "applicant's disclosure of his or her own work within the year before the application filing date cannot be used against him or her under 35 U.S.C. 102(a)." M.P.E.P. §2131.01.

Furthermore, and with respect to point 3 above, the anti-viral activity of interferon-τ was evaluated *in vivo* by inoculating 24 newborn lambs with ovine lentivirus and treating the lambs with interferon-τ, as reported in Applicants' specification on page 35, lines 11-30. The lambs treated with interferon-τ had a reduced blood viral titer relative to animals not treated with interferon-τ (page 35, lines18-20).

According to the M.P.E.P. § 2164.02, a rigorous or an invariable exact *in vitrolin vivo* correlation is not required (citing to *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985). As stated in *Cross*: "based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary, where the disclosure of pharmacological activity is reasonably based upon the probative evidence."

In the present claims, a method of inhibiting viral replication by contacting cells infected with a virus with a dose of interferon-τ of at least about $5x10^4$ U/day is recited. The anti-viral activity of interferon-τ is clearly established by the *in vitro* data and by the *in vivo* data. The cellular assays are the same as assays used in the published literature.

In light of the data present in the specification in support of the claims, Applicants respectfully request that the Examiner withdraw the rejection.

2. The Examiner's Second Assertion

The Examiner asserts that "the therapeutic effect of ovine interferon-τ therapy can be species and model-dependent."

Applicants are unaware of any document that supports this assertion. Nor has the Examiner provided a reference to support this argument. If the Examiner is aware of a teaching to support this, Applicants are entitled to a copy for review.

3. The Examiner's Third Assertion

The Examiner also asserts that there is no guidance provided in the specification in choosing the therapeutically effective amount for administering interferon-τ to treat various viral replications (Office action, paragraph bridging pages 3-4). That is

because there are no *in vivo* working examples, the invention lacks operability, and there is insufficient disclosure to reasonably predict that interferon-τ could be used to treat a viral infection *in vivo* (Office action, paragraph bridging pages 3-4). Moreover, it is unclear to the Examiner if the dose indicated would be sufficient for inhibiting both HIV and Hepatitis B viral infections.

As noted above, *in vivo* data is provided on page 35, lines 11-22 of the specification.

With respect to the Examiner's concern that the dose indicated would be sufficient for inhibiting both HIV and hepatitis B viral infections, Applicants note that the standard for enablement is that the specification describe "how to make and how to use the invention." M.P.E.P. § 2164. The present invention is directed to a method of inhibiting viral replication by contacting cells infected with a virus with a dose of interferon-τ of at least about $5x10^4$ U/day is recited. A person of skill in the art is taught how to make the invention by the teachings in the specification on providing interferon-τ and preparing it for contact with cells. A person of skill in the art is taught how to use the invention by the teachings in the specification on how to contact a cell, *in vitro* or *in vivo*, with a dose of interferon-τ.

Claim 1 specifies a minimum dose of interferon-τ to be provided to the infected cell. The dosage was determined based on the studies described above, as well as the other studies reported in the specification, and on the finding that interferon-τ has a low cytotoxicity. As discussed on page 57, line 32 to page 58, line 10, the low toxicity of the protein permits administration at doses higher than that for other interferons.

In accord with M.P.E.P. § 2164.04, Applicants submit that the specification contains a teaching of the manner and process of making and using the invention in terms that correspond to in scope to the claims. This teaching must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph unless there is a reason to doubt the objective truth of the statements. The Examiner has given no reason to doubt the truth of the teachings in the specification.

4. The Examiner's Fourth Assertion

The Examiner further asserts that "there is often no known correlation between *in vitro* and *in vivo* results, because the artisan recognizes that an *in vitro* assay cannot duplicate the complex conditions of *in vivo* treatment." (Office Action, page 4, first full paragraph). The Examiner continues, stating that "pharmaceutical therapies are unpredictable" and lists four reasons for the unpredictability. Thus, according to the Examiner, since Applicant has not provided any working examples of the efficacy using ovine interferon-τ in treating already established disease subjects viral infection (sic), it would require undue experimentation to practice the claimed invention, and that there is no reasonable expectation of success in transferring the *in vitro* method to treat viral infections. (Office Action, page 5, first full paragraph).

As discussed above, Applicants specification provides analysis of antiviral activity of interferon-τ in Madin-Darby bovine kidney (MDBK) cells using vesicular stomatitis virus as the challenge virus (see Example 2 on page 63 and Example 10 on page 79 of the specification), in sheep normal fibroblasts cells using vesicular stomatitis virus as the challenge virus (see Example 10 on page 79), in peripheral blood mononuclear cells infected with feline immunodeficiency retrovirus (Examples 11 and 12, pages 80, 82), and HepG2-T14 cells infected with hepatitis B (Example 18, pages 98-101). The anti-viral activity of interferon-τ was evaluated *in vivo* by inoculating 24 newborn lambs with ovine lentivirus and treating the lambs with interferon-τ (page 35, lines 11-30).

In light of the ample data provided in the specification, the Examiner's assertion cannot stand, and withdrawal of the rejection of the claims is respectfully requested.

B. Rejection of Claim 67 as Non-Enabled

The Examiner asserts that while the specification is enabling for inhibiting HIV virus replication, it does not reasonably provide enablement for inhibiting hepatitis C viral replication. The lack of working examples for inhibition of hepatitis C virus translates into undue experimentation to make and use the claimed method – since no guidance as to cell lines or amount of interferon for inhibition of hepatitis C viral replication is given. (Office Action, page 6, first and second full paragraphs).

The specification is replete with examples of suitable cell lines and assay for testing the anti-viral activity of interferon-τ (see the summary of *in vitro* data above in A.4.). In light of these examples, it is hard to imagine that a person of skill in the art would be unable to select a cell line, infect the cells with hepatitis C virus, and contact the cells with a dose of interferon-τ in the dose set forth in the claim or at a dose selected based on the guidance in the specification. If the Examiner can establish that one of skill in the art would be unable to conduct what is a routine test for those involved in *in vitro* testing of therapeutic agents, the Applicants would like to review any evidentiary support.

Accordingly, withdrawal of the rejection of claim 67 under 35 U.S.C. § 112, first paragraph is respectfully requested.

III. Conclusion

Applicants submit that the claims are now in condition for allowance, and a Notice of Allowance is respectfully requested. The Examiner is invited to call the undersigned at (650) 838-4402 as needed.

Respectfully submitted,

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